



DEPARTMENT OF THE AIR FORCE
59TH MEDICAL WING (AETC)
JOINT BASE SAN ANTONIO - LACKLAND TEXAS

9 MAY 2016

MEMORANDUM FOR SGOBV

ATTN: MAJ CHRISTOPHER MONNIKENDAM

FROM: 59 MDW/SGVU

SUBJECT: Professional Presentation Approval

1. Your paper, entitled **Early Hyponatremia is Associated with Increased Mortality in Extremely Low Birth Weight (ELBW) Infants** presented at/published to **Pediatric Academic Societies Meeting, Baltimore, MD 30 APR 2016 – 3 MAY 2016** with MDWI 41-108, and has been assigned local file #**16189**.
2. Pertinent biographic information (name of author(s), title, etc.) has been entered into our computer file. Please advise us (by phone or mail) that your presentation was given. At that time, we will need the date (month, day and year) along with the location of your presentation. It is important to update this information so that we can provide quality support for you, your department, and the Medical Center commander. This information is used to document the scholarly activities of our professional staff and students, which is an essential component of Wilford Hall Ambulatory Surgical Center (WHASC) internship and residency programs.
3. Please know that if you are a Graduate Health Sciences Education student and your department has told you they cannot fund your publication, the 59th Clinical Research Division may pay for your basic journal publishing charges (to include costs for tables and black and white photos). We cannot pay for reprints. If you are 59 MDW staff member, we can forward your request for funds to the designated wing POC.
4. Congratulations, and thank you for your efforts and time. Your contributions are vital to the medical mission. We look forward to assisting you in your future publication/presentation efforts.

Linda Steel-Goodwin

LINDA STEEL-GOODWIN, Col, USAF, BSC
Director, Clinical Investigations & Research Support

PROCESSING OF PROFESSIONAL MEDICAL RESEARCH/TECHNICAL PUBLICATIONS/PRESENTATIONS

INSTRUCTIONS

USE ONLY THE MOST CURRENT 59 MDW FORM 3039 LOCATED ON AF E-PUBLISHING

1. The author must complete page two of this form:
 - a. In Section 2, add the funding source for your study [e.g., 59 MDW CRD Graduate Health Sciences Education (GHSE) (SG5 O&M); SG5 R&D; Tri-Service Nursing Research Program (TSNRP); Defense Medical Research & Development Program (DMRDP); NIH; Congressionally Directed Medical Research Program (CDMRP) ; Grants; etc.]
 - b. In Section 2, there may be funding available for journal costs, if your department is not paying for figures, tables or photographs for your publication. Please state "YES" or "NO" in Section 2 of the form, if you need publication funding support.
2. Print your name, rank/grade, sign and date the form in the author's signature block or use an electronic signature.
3. Attach a copy of the 59 MDW IRB or IACUC approval letter for the research related study. If this is a technical publication/presentation, state the type (e.g. case report, QA/QI study, program evaluation study, informational report/briefing, etc.) in the "Protocol Title" box.
4. Attach a copy of your abstract, paper, poster and other supporting documentation.
5. Save and forward, via email, the processing form and all supporting documentation to your unit commander, program director or immediate supervisor for review/approval.
6. On page 2, have either your unit commander, program director or immediate supervisor:
 - a. Print their name, rank/grade, title; sign and date the form in the approving authority's signature block or use an electronic signature.
7. Submit your completed form and all supporting documentation to the CRD for processing (59crdpubspres@us.af.mil). If you have any questions or concerns, please contact the 59 CRD/ Publications and Presentations Section at 292-7141 for assistance.
8. The 59 CRD/Publications and Presentations Section will route the request form to clinical investigations, 502 ISG/JAC (Ethics Review) and Public Affairs (59 MDW/PA) for review and then forward you a final letter of approval or disapproval.
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NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement:

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NOTE: All abstracts, papers, posters, etc., should contain the following disclaimer statement for research involving humans:

"The voluntary, fully informed consent of the subjects used in this research was obtained as required by 32 CFR 219 and DODI 3216.02_AFI 40-402."

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"The experiments reported herein were conducted according to the principles set forth in the National Institute of Health Publication No. 80-23, Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1966, as amended."

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TO: Clinical Research Division 59 MDW/CRD Contact 292-7141 for email instructions.	22. DATE RECEIVED 4/26/2016	23. ASSIGNED PROCESSING REQUEST FILE NUMBER 16189	
24. DATE REVIEWED 29 Apr 2016		25. DATE FORWARDED TO 502 ISG/JAC	
26. AUTHOR CONTACTED FOR RECOMMENDED OR NECESSARY CHANGES: <input checked="" type="checkbox"/> NO <input type="checkbox"/> YES If yes, give date. _____ <input type="checkbox"/> N/A			
27. COMMENTS <input checked="" type="checkbox"/> APPROVED <input type="checkbox"/> DISAPPROVED The poster presentation is approved.			
28. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Rocky Calcote, PhD, Clinical Res. Administrator		29. REVIEWER SIGNATURE CALCOTE.ROCKY.D.11782458 <small>44</small> <small>Digitally signed by CALCOTE.ROCKY.D.1178245844 DN: cn=US, ou=U.S. Government, ou=DoD, ou=PR, ou=USAF, email=ALCOTE.ROCKY.D.1178245844 Date: 2016.04.29 06:17:31 -0500</small>	30. DATE
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40. PRINTED NAME, RANK/GRADE, TITLE OF REVIEWER Christopher Carwile, TSgt/E-6, NCOIC, PA		41. REVIEWER SIGNATURE CARWILE.CHRISTOPHER.STE WART.1280477229 <small>Digitally signed by CARWILE.CHRISTOPHER.STE DN: cn=US, ou=U.S. Government, ou=DoD, ou=PR, ou=USAF, cn=CARWILE.CHRISTOPHER.STE WART.1280477229 Date: 2016.05.03 10:22:00 -0500</small>	42. DATE 3 May 2016
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Early Hypertremia is Associated with Increased Mortality in Extremely Low Birth Weight (ELBW) Infants

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Background:

ELBW infants are at high risk for increased and variable insensible fluid losses and associated co-morbidities. Early fluid restriction in older preterm infants is associated with decreased mortality and co-morbidities. Mild hypertremia is often targeted or tolerated with this strategy. Although this fluid restriction strategy is often used in the ELBW population, the association between early serum sodium levels and ELBW neonatal outcomes has not been well evaluated. Our objective is to investigate the relationship between mean serum sodium in the first 5 days of life and complications of prematurity in ELBW infants.

Objective:

To investigate the relationship between mean serum sodium in first 5 days of life and common complications of prematurity in ELBW infants from 2004-2014.

Design/Methods:

Utilizing a retrospective cohort design we identified a subset of NICU infants less than 1000g birth weight and between 23 and 29 weeks gestational age. Data were extracted from the Pediatric Clinical Data Warehouse, a de-identified national dataset that includes infants cared for at Pediatric managed NICUs. Across all eligible facilities we identified 26,871 infants who met stated criteria. From this, patients were excluded for incomplete serum sodium documentation, 12,437 infants remained and these data were subjected to further analyses. Mean serum sodium levels over day of life 1-5 were determined. Infants with mean normal mean serum sodium levels (135-144mEq/dL) were directly compared to infants with serum sodium levels above and below the normal range. The companion groups used were as follows: <125mEq/dL, 125-134mEq/dL, 145-154mEq/dL. Evaluation of the primary outcome of mortality and secondary outcomes of grade 3 and 4 IVH, stage 4 and surgical ROP, BPD, medical/surgical NEC, PDA ligation, PDA diagnosis, and renal insufficiency were performed. Subgroup analyses comparing outcomes of different gestational ages between the normal serum sodium range group and a mildly hypertremic group were also performed. Statistical analyses was performed utilizing Student's t-Test, Chi square with continuity correction, Wilcoxon Rank-Sum Test.

Results:

Infants with mild to severe hypertremia tended to be younger and smaller, have lower Apgar scores, and have received an incomplete course of antenatal steroids. The normal serum sodium group had significantly lower mortality compared to all other groups except the lowest serum sodium group (<125mEq/dL) which only included 3 infants. All secondary outcomes were significantly higher in the mildly hypertremic group and mild hyponatremia was associated with significantly increased incidences of IVH, NEC, and PDA diagnosis. There was no association with improved secondary outcomes in any group as compared to the normal serum sodium group. Subgroup analysis by gestational age comparing the normal serum sodium group to the mildly hypertremic group showed a significant increase in mortality within the 24 week [30.8% vs 24.8%, p<0.003] and 25 week [16.8% vs 14%, p<0.001] mildly hypertremic subgroups.

Serum Sodium vs Outcomes All Gestational Age Compared to 135-144 mEq/dL Group

	<125	125-134	135-144	145-154	≥155
Mortality	33.3	** 20.3	12.9	** 21.6	** 80.4
IVH Grade 3-4	33.3	** 20.3	10.6	** 18.4	** 51.7
Stage 4 and Surgical ROP	0	5.7	12.5	** 14.9	** 7.1
BPD	0	38.2	38.9	** 43.5	28.8
Medical/Surgical NEC	0	** 15.3	14.2	** 16.5	** 13.3
PDA Ligation	0	15.9	15.8	** 18.3	18.3
PDA	66.7	** 76.4	70.8	** 76.3	73.3
Diagnosis Renal Insufficiency*	0	0.29	3.1	1.7	0.21

*Creatinine >1.3 on day of life 3

No significantly lower incidence of any outcome when compared to the normal serum sodium group.

Demographics

	<125	125-134	135-144	145-154	≥155
Sample Size	3	365	9670	2339	60
Gestational Age (weeks)	27 (26-27)	26 (24-28)	26 (24-28)	* 25 (23-27)	* 24 (23-25)
Birth Weight (grams)	736	773	774	* 704	* 595
Female Gender (%)	66.7	51.5	53	* 46.9	45
APGAR 1 Minute (median, 10-90%)	6 (5-8)	6 (5-8)	7 (5-8)	* 4 (1-7)	* 3 (1-6)
APGAR 5 Minute (median, 10-90%)	7 (6-9)	7 (4-9)	7 (5-9)	* 7 (3-9)	* 6 (2-8)
Antenatal Steroids (%)	100	* 76.4	84	* 80.7	* 68.3

* p < 0.05 ** p < 0.01

Serum Sodium vs Outcomes Gestational Age 24 weeks

	135-144	145-155	p value
Total Subjects	1500	721	—
Mortality	* 372 (24.8%)	222 (30.8%)	* 0.003
IVH Grade 3-4	281 (18.7%)	151 (20.9%)	0.240
Treated ROP	216 (14.4%)	94 (13.0%)	0.422
BPD	692 (46.1%)	360 (49.9%)	0.103
Medical/Surgical NEC	176 (11.7%)	83 (11.5%)	0.935
Treated PDA	1266 (84.4%)	603 (83.6%)	0.689

Significantly lower mortality in the normal serum sodium group.

Serum Sodium vs Outcomes Gestational Age 25 weeks

	135-144	145-155	p value
Total Subjects	2064	684	—
Mortality	* 288 (14.0%)	115 (16.8%)	* <0.001
IVH Grade 3-4	409 (19.8%)	132 (19.3%)	0.811
Treated ROP	196 (9.5%)	72 (10.5%)	0.476
BPD	940 (45.5%)	309 (45.2%)	0.902
Medical/Surgical NEC	221 (10.7%)	80 (11.7%)	0.518
Treated PDA	* 1648 (79.8%)	517 (75.6%)	* 0.021

Significantly lower mortality in the normal serum sodium group.

Conclusions:

In our sample population we found that average serum sodium levels within the first 5 days of life in ELBW infants outside the normal range are associated with increased mortality. This association was still present in a subgroup analysis of 24 and 25 week gestation infants. Further studies are warranted to evaluate the clinical relevance of this association.

Future Directions:

- Initial serum sodium level as prognostic indicator of ELBW mortality
- Serum sodium levels and outcomes in relation to gestational age, birth weight, and weight trends over the first 5 days of life
- Multivariate analysis is ongoing to investigate the clinical relevance of these associations

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